REMARKS

Claims 1, 9 to 13, 16, 17, 21 to 23, 26 to 31, 37, 38, 41 to 60, 62 to 66, 81, and 87 to 89 are currently pending in the instant application. Claims 67 to 79, 80, and 82 to 85 have been withdrawn. Claims 2 to 8, 14, 15, 18 to 20, 24, 25, 32 to 36, 39, 40, 61, and 86 have been cancelled without prejudice or disclaimer.

Claim 1 has been amended to recite in pertinent part that "linker –B–C– is an optionally substituted linker of the formula $–CH_2(CH_2)_z–$, where z is 1 or 2;" "R_1 is optionally substituted aryl or heterocyclyl;" "R_2 is selected from $–C(O)R_3$ and $–C(O)N(R_4)R_3$;" and "X is O." Support for the amendments can be found, *e.g.*, on page 14, lines 8 to 11, and page 15, lines 8 to 11; and in original claims 19, 20, 24, and 25 of the corresponding PCT publication (WO 2005/061513, "the 513 publication").

Claim 13 has been amended to recite in pertinent part that "R_2 is selected from $–C(O)R_3$ and $–C(O)N(R_4)R_3$." Support for the amendment can be found, *e.g.*, on page 14, lines 8 to 11, and page 15, lines 8 to 11 of the '513 publication.

Claim 26 has been amended to recite in pertinent part that "R_1 represents phenyl, thienyl, pyrrolyl, pyridyl, or pyridyl." Support for the amendment can be found, *e.g.*, in original claim 26.

Claim 38 has been amended to recite in pertinent part that "A, together with the atoms to which it is attached, represents an optionally substituted pyridyl;" and "R_3 is selected from $–(CH_2)_mC_{3-7}$ cycloalkyl, $–(CH_2)_mC_{4-7}$ cycloalkenyl, $–(CH_2)_m$ aryl, $–(CH_2)_m$ arylC_{1-12} alkyl, $–(CH_2)_m$ arylC_{2-12} alkenyl, $–(CH_2)_m$ arylC_{2-12} alkynyl and $–(CH_2)_m$ heterocyclyl." Claim 38 has further been amended by deleting the provisos from the claim. Support for the amendment can be found, *e.g.*, in original claim 38.

Claim 44 has been amended to recite in pertinent part that "R_3 is selected from $–(CH_2)_mC_{3-7}$ cycloalkyl, $–(CH_2)_mC_{4-7}$ cycloalkenyl, $–(CH_2)_m$ aryl, $–(CH_2)_m$ arylC_{1-12} alkyl, $–(CH_2)_m$ arylC_{2-12} alkenyl, $–(CH_2)_m$ arylC_{2-12} alkynyl and $–(CH_2)_m$ heterocyclyl." Support for the amendment can be found, *e.g.*, in original claim 44.

Claim 65 has been amended by listing the compounds in Table 3 by their chemical names. Support for the amendment can be found, *e.g.*, in Table 3 of the '513 publication.

Claims 16, 41, and 42 have been amended solely for clarity, without prejudice or disclaimer.

Claims 87 to 89 are new. Support for claims 87 to 89 can be found, *e.g.*, on page 14, lines 8 to 17 of the '513 publication.

Applicants reserve the right to pursue the subject matter of unclaimed subject matter in the instant application in one or more divisional, continuation, and/or continuation in part applications. Applicants submit that the instant claims are fully supported by the specification as filed originally, and no new matter has been introduced.

A. <u>The Rejection under 35 U.S.C. § 112, First Paragraph, against Claims 1, 2, 9 to 31, and 35 to 37 Should Be Withdrawn</u>

In the Office Action, claims 1, 2, 9 to 31, and 35 to 37 stand rejected under 35 U.S.C. §112, first paragraph, allegedly for lack of enablement for some compounds of Formula I. Therefore, the rejection is hereby respectfully traversed.

In making an enablement rejection, the Examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure. *In re Wright,* 999 F.2d 1557, 1562 (Fed. Cir. 1993). Furthermore, a "specification disclosure which contains a teaching of the manner and process of making and using an invention…must be taken as being in compliance with the enablement requirement…unless there is a reason to doubt the objective truth of the statement contained therein which must be relied on for enabling support." *In re Marzocchi*, 439 F.2d 220, 224 (CCPA 1971). "It is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." 439 F.2d at 224.

As discussed previously in the response to the May 26, 2010 Office Action, the scope of the instant claims enabled by the instant specification is much broader than that acknowledged by the Office Action. In spite of the biological data disclosed in the instant specification and the evidence presented in the previous response to rebut this lack of enablement rejection, the Office Action maintains the rejection and acknowledges only that the instant claims are enabled for

"treating the viral infection with compound [sic] defined by formula I, wherein A is prydiyl [sic], R1 is a phenyl or substituted phenyl, and R2 is COR3 wherein R3 is optionally substituted aryl, X is oxygen." *See*, Item 8 on page 3 of the Office Action. Thus, the Office Action fails to give full consideration of the arguments and evidence presented in the response to the May 26, 2010 Office Action. *In re Soni*, 54 F.3d 746, 750 (Fed. Cir. 1995) (error not to consider evidence presented in the specification); MPEP §2145.

For example, the Office Action fails to consider the facts presented in the previous response to the Office Action that compounds 363-370, 377, 379, 381, 382, 385-387, 391, 392, 394, 395, 397-401, 404-406, 408, 409, 412-416, 420-423, 430, 431, 434, 436-438, 441, 442, 444, 445, 448-450, 453-458, 461-465, 467, 468, 474, and 480-484 in Tables 3 and 7, each of which has R_2 as $-COR_3$ and R_3 as optionally substituted heterocyclyl, have been shown to be active against RSV A2. *See* Table 7 on pages 96 and 97 of the '513 publication.

The allegations, made by the Office Action in response to the evidence previously presented, that compounds 351 and 371 "only show very weak antiviral activity" and that "[o]ne of ordinary skill in the art would have no reasonable expectation that such compounds would be useful for treating RSV viral infections" are simply unfounded. Compounds 351 and 371 in Tables 3 and 7 are nonlimiting examples of compounds of Formula I, where R^1 is optionally substituted phenyl, R_2 is $-COR_3$, R_3 is $-(CH_2)_m$ aryl, and X is oxygen.

"Courts have repeatedly found that the mere identification of a pharmacological activity of a compound that is relevant to an asserted pharmacological use provides an "immediate benefit to the public" and thus satisfies the utility requirement," and as well as the enablement requirement. MPEP 2107.01(III) (citing *Nelson v. Bowler*, 626 F.2d 853, 856 (CCPA 1980)) and MPEP 2164.06(a)(III). "The Federal Circuit has reiterated that therapeutic utility sufficient under the patent laws is not to be confused with the requirements of the FDA with regard to safety and efficacy of drugs marketed in the United States. MPEP 2107.01(III) and MPEP 2164.06(a)(III) (Emphasis added). "Office personnel should not construe 35 U.S.C. 101, under the logic of "practical" utility or otherwise, to require that an applicant demonstrate that a therapeutic agent based on a claimed invention is a safe or fully effective drug for humans." MPEP 2107.01(III) and MPEP 2164.06(a)(III). Therefore, unless the Office Action can back up assertions of its own with acceptable evidence or reasoning as to why one of ordinary skill in the art would have no reasonable expectation that such compounds would be useful for treating RSV

viral infections, "there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." *In re Marzocchi*, 439 F.2d 220, 224 (CCPA 1971).

Furthermore, it is immaterial that the antiviral activity of compounds 123, 337, 339, 342, 345, 450, 354, 356, 362, 374, and 341 has not been disclosed, because these compounds are outside the scope of the instant claims. It is also immaterial that the antiviral activity of compounds 343, 346, 348, 349, and 373, wherein R_3 is $-(CH_2)$-aryl, has not been reported. There are simply no such requirements that the activity of every single compound disclosed in a patent application has to be described. More importantly, compounds 351 and 371, as examples of the compounds where R_3 is $-(CH_2)_m$ aryl, to which compounds 343, 346, 348, 349, and 373 belong, have been shown to be active against RSV A2.

Thus, the instantly claimed methods are fully enabled and the rejection has been overcome. Therefore, Applicants respectfully request that this rejection be withdrawn.

Although Applicants strongly disagree with the Examiner's allegation, instant claim 1 has been amended to specifically recite in pertinent part that "R_1 is optionally substituted aryl or heterocyclyl;" "R_2 is selected from $-C(O)R_3$ and $-C(O)N(R_4)R_3$;" and "X is O;" solely to expedite the prosecution and allowance of the instant application.

B. <u>The Rejection under 35 U.S.C. § 103(a) against Claims 33, 38, 39, 41 to 60, 62 to 66, 81, and 86 Should Be Withdrawn</u>

In the Office Action, claims 33, 38, 39, 41 to 60, 62 to 66, 81, and 86 stand rejected under 35 U.S.C. §103(a), allegedly as being unpatentable over Bamba *et al.* (WO 02/066479, "Bamba"). In particular, the Office Action alleges that "the compounds herein claimed encompass at least part of the compounds within the general formula disclosed in Bamba;" and "[t]therefore, one of ordinary skill in the art, need no more motivation other than following the instruction provided by Bamba to make the compounds herein claimed." Applicants respectfully disagree.

"The determination of obviousness is a matter of law based on findings of underlying fact, wherein the factors identified in *Graham v. John Deere Co.*, . . . guide the inquiry . . . ." *Sanofi-Synthelabo, Inc. v. Apotex, Inc.*, 550 F.3d 1075, 1085 (Fed. Cir. 2008), citing *Graham v. John Deere Co.*, 383 U.S. 1 (1966); *see also KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 399

(2007). The factors identified in *Graham* are: (1) "the scope and content of the prior art;" (2) "the differences between the prior art and the claims;" (3) "the level of ordinary skill in the pertinent art;" and (4) "secondary considerations." *Graham*, 383 U.S. at 17–18. "A patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR*, 550 U.S. at 401. It is important to identify "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *Id.*

To establish a *prima facie* case of obviousness of new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner. *Takeda Chem. Indus. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. 2007). Furthermore, support for a proper *prima facie* case of obviousness of a new compound based on structural similarity of a prior art compound requires the identification of a reason as to why one of ordinary skill in the art would *select* and *modify* a known compound in a particular way to achieve the claimed compound. *Eisai Co. Ltd. v. Dr. Reddy's Labs., Ltd.*, 533 F.3d 1353, 1357 (Fed. Cir. 2008) (emphasis added). Even in light of *KSR*, the Federal Circuit has maintained that the chemical arts are often unpredictable, such that *KSR*'s focus on "identified predictable solutions" may present a difficult hurdle to overcome because potential solutions in the chemical arts are less likely to be genuinely predictable. *Procter & Gamble Co. v Teva Pharms. USA, Inc.*, 566 F.3d 989, 996 (Fed. Cir. 2009). Thus, in order to establish a proper *prima facie* case of obviousness based on structural similarity, the Examiner must identify: (1) why one of ordinary skill in the art would have selected a particular compound from the cited reference as a lead compound; and (2) why one of ordinary skill in the art would have modified that particular compound in a particular way to arrive at the instantly claimed compounds. *Eisai Co. Ltd. v. Dr. Reddy's Labs., Ltd.*, 533 F.3d 1353, 1357 (Fed. Cir. 2008).

The Office Action fails to establish a *prima facie* case of obviousness for at least the reasons discussed herein.

As discussed previously, the instant claims are directed toward compounds that are useful in treating RSV infections and methods for treating RSV infections. However, Bamba *et al.* disclose compounds for treating diabetes. *See*, the English abstract of the '479 publication. Bamba *et al.* are completely silent as to the treatment of viral infections, let alone the treatment of RSV infections. *See*, the English abstract of the '479 publication.

The Office Action fails to articulate why one of ordinary skill in the art would have been motivated to select any possible compounds in Bamba *et al.*, none of which had been shown to be active against RSV at the time of its disclosure, to arrive at the instantly claimed compounds that are active against RSV infections. "The fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a prima facie case of obviousness." MPEP 2144.08 (citing *In re Baird*, 16 F.3d 380 (Fed. Cir. 1994)). It remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner. *Takeda Chem. Indus. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. 2007).

Furthermore, it is well established that the chemical arts are often unpredictable, and the modification of a lead compound often leads to different activity. *Procter & Gamble Co. v Teva Pharms. USA, Inc.*, 566 F.3d 989, 996 (Fed. Cir. 2009). Thus, without the teaching of the instant application, one skilled in the art would have no reasonable expectation from the disclosure of Bamba *et al.* that the instant compounds could be active against RSV and useful for treating RSV infections. In this regard, the Office Action is impermissibly using hindsight reconstruction in its allegation of obviousness.

The allegation in the Office Action that "the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious" begs the question. Since the instant claims are directed to often unpredictable chemical arts, the Office Action fails to articulate how "another advantage" "would flow naturally from the following the suggestion of the prior art." Additionally, the Office Action also fails to articulate how "the differences would otherwise be obvious" to one of ordinary skill in the art. As a matter of fact, there is currently no effective treatment for respiratory syncytial virus (RSV) infection, to which the instant application is directed.

Therefore, the instant claims are not *prima facie* obvious, and reconsideration and withdrawal of the rejection are respectfully requested.

SUMMARY

Should the Examiner believe that prosecution of this application might be expedited by further discussion of any remaining issue, the Examiner is cordially invited to contact the undersigned representative of Applicants, Dale L. Rieger, Ph.D., by phone at (858) 314-1200 or by email at drieger@jonesday.com.

Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 50-3013 and please credit any excess fees to such deposit account.

Respectfully submitted,

Dated: February 8, 2011

By: 
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Signed for

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